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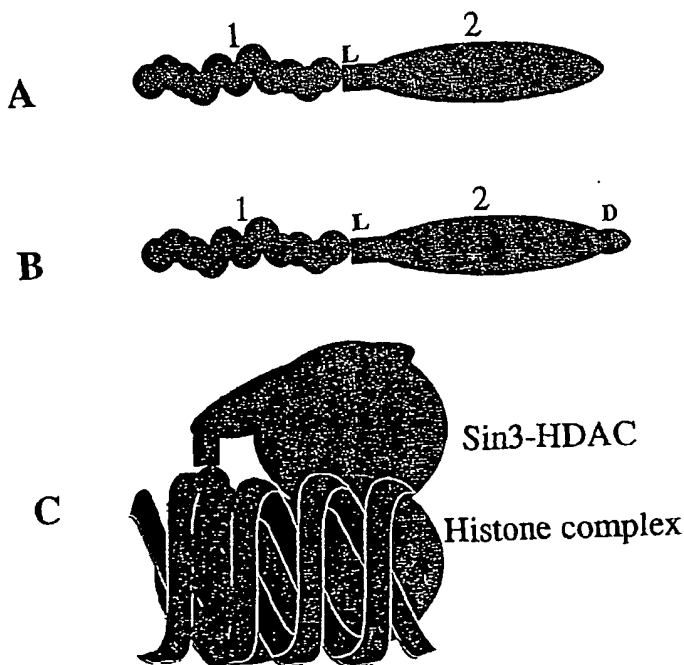
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(54) Title: CONTROL OF APOPTOSIS USING A COMPLEX OF AN OLIGONUCLEOTIDE AND A REGULATORY PEPTIDE



(57) Abstract: A method for suppressing the expression of a selected apoptosis-related gene in a cell the method comprising introducing into the cell a molecule comprising (1) a nucleic acid binding portion which binds to a site at or associated with the selected gene which site is present in a genome and (2) a modifying portion, wherein the nucleic acid binding portion comprises an oligonucleotide or oligonucleotide mimic or analogue, and wherein the repressor portion comprises a polypeptide or peptidomimetic. Molecules for use in the methods of the invention are provided. The repressor or modifying portion may be a portion of a histone deacetylase or DNA methylase or polypeptide capable of recruiting a histone deacetylase or DNA methylase. The nucleic acid binding portion may be a triplex forming oligonucleotide (TFO). The apoptosis-related gene may be Bcl-2. The methods and molecules may be useful in the treatment of cancer.

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INTERNATIONAL SEARCH REPORT

International Application No
GB 03/05321

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/63 C12N15/11 C12N5/10 C07K14/47 A61K38/17
A01K67/027 A01H5/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 03/033701 A (PUFONG BORIS TUMI ; ALI SIMAK (GB); BULUWELA LAKI (GB); KANDA PATRICK) 24 April 2003 (2003-04-24) examples 1-13	1-47
P, X	WO 03/010308 A (ALI SIMAK ; HOLMES DAVID (GB); WAXMAN JONATHAN (GB); BULUWELA LAKJAYA) 6 February 2003 (2003-02-06) examples 1-6	1-47
X	WO 01/83793 A (SANGAMO BIOSCIENCES INC) 8 November 2001 (2001-11-08) page 17, line 10 - line 17 page 21, line 17 - line 18 page 31, line 11 - line 20 page 32, line 1 - line 5 page 32, line 23 - line 26 page 35, line 26 - line 27	1-47

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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/26960 A (SANGAMO BIOSCIENCES INC) 4 April 2002 (2002-04-04) page 25, line 32 - page 26, line 8 page 29, line 1 - line 15 page 31, line 10 - line 14 page 31, line 24 - line 26; example 4	1-14, 18-47
Y	-----	15-17
Y	WO 01/02019 A (IMP COLLEGE INNOVATIONS LTD ; ALI SIMAK (GB); BULUWELA LAKJAYA (GB)) 11 January 2001 (2001-01-11) the whole document	15-17
X	----- WO 02/31166 A (CROSSLINK GENETICS CORP) 18 April 2002 (2002-04-18) page 14, line 5 - page 16, line 7 page 19, line 10 - line 15; figures 1,2 -----	1-4, 7-13, 20-47

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 03/05321

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 29 and 46 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 03033701	A	24-04-2003	WO 03033701 A1 GB 2382581 A	24-04-2003 04-06-2003
WO 03010308	A	06-02-2003	WO 03010308 A2 GB 2380195 A	06-02-2003 02-04-2003
WO 0183793	A	08-11-2001	AU 5391401 A AU 5574801 A AU 5587001 A AU 5733101 A AU 5742101 A CA 2407460 A1 CA 2407695 A1 CA 2407745 A1 EP 1276859 A2 EP 1276865 A2 EP 1276860 A2 GB 2365969 A GB 2365011 A JP 2003531616 T WO 0183819 A2 WO 0183751 A2 WO 0184148 A2 WO 0183793 A2 WO 0183732 A2 US 2003129603 A1 US 2003049649 A1 US 2003190664 A1 US 2002127559 A1 US 2002076711 A1 US 2002081603 A1 US 2002115215 A1 US 2002064802 A1	12-11-2001 12-11-2001 12-11-2001 12-11-2001 12-11-2001 08-11-2001 08-11-2001 08-11-2001 22-01-2003 22-01-2003 22-01-2003 27-02-2002 13-02-2002 28-10-2003 08-11-2001 08-11-2001 08-11-2001 08-11-2001 08-11-2001 10-07-2003 13-03-2003 09-10-2003 12-09-2002 20-06-2002 27-06-2002 22-08-2002 30-05-2002
WO 0226960	A	04-04-2002	AU 1343102 A WO 0226960 A2 US 2003082552 A1	08-04-2002 04-04-2002 01-05-2003
WO 0102019	A	11-01-2001	AU 5556600 A CA 2376166 A1 EP 1190073 A2 WO 0102019 A2 GB 2367555 A JP 2003503082 T	22-01-2001 11-01-2001 27-03-2002 11-01-2001 10-04-2002 28-01-2003
WO 0231166	A	18-04-2002	AU 1170302 A CA 2425917 A1 EP 1356061 A2 WO 0231166 A2 US 2003105045 A1	22-04-2002 18-04-2002 29-10-2003 18-04-2002 05-06-2003